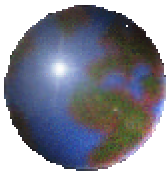


## *Select Agents in Product Development*

- ❑ **Continual updates regarding Terrorism concerns**
  - ❑ <http://www.bt.cdc.gov/agent/index.asp>
  - ❑ Agents, Diseases and Threats
    - ❑ Chemical
    - ❑ Radiation
    - ❑ Biological
  - ❑ Select Agents within Biological Category
    - ❑ <http://www.cdc.gov/od/sap/general.htm>
    - ❑ <http://www.cdc.gov/od/sap/appen1.htm>
    - ❑ <http://www.cdc.gov/od/sap/docs/42cfr73.pdf>
- ❑ **Awareness of these regulations in product development**



# *Origins of Select Agent Regulations*

## **❑ First Biological Select Agent Regulation, 42 CFR 72.6**

### **❑ Proposed June 10, 1996, by CDC and HHS**

- ❑ Notice of Proposed Rulemaking to implement Section 511 of Public Law 104-132, "The Antiterrorism and Effective Death Penalty Act of 1996"

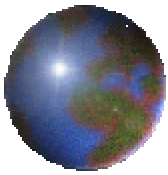
- ❑ Requires the Secretary of HHS to regulate the transfer of select agents; delegated responsibility to CDC

### **❑ Effective date April 15, 1997**

- ❑ Registration of facilities/supporting documentation

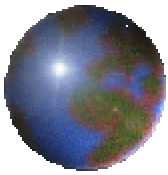
- ❑ List of Select Agents

- ❑ Mechanism for possible exemptions



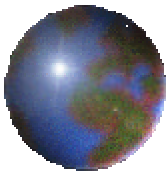
# *Current Biological Select Agent Rule*

- ❑ **Interim Final Rule 42 CFR part 73**
  - ❑ Possession, Use and Transfer of Select Agents and Toxins; Interim Final Rule
- ❑ **Co-published with 42 CFR part 1003**
  - ❑ Established monetary penalties for violations
- ❑ **Significant dates**
  - ❑ Published Friday December 13, 2002
  - ❑ Effective February 7, 2003 (phased in timelines for some aspects)
  - ❑ Comment deadline February 11, 2003
  - ❑ Full compliance by October 11, 2003



# ***Purpose of the Select Agent Update***

- ❑ **42 CFR 72.6**
  - ❑ Transfers/shipping/sending/receiving SA in the USA
- ❑ **42 CFR 73 (2001 Anthrax)**
  - ❑ Possession, use and transfer within USA, receipt from outside US
  - ❑ Additional requirements/security risk assessments
  - ❑ Bolstered authority to protect against misuses of Select Agents and Toxins whether inadvertent or as a result of terrorist acts against US homeland.



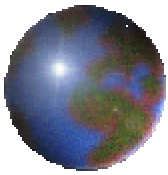
# ***“Reducing the Chance of Accidental or Intentional Release”***

## **❑ 42 CFR 73 Critical Requirements**

- ❑ Register/determine where select agents and toxins are located
- ❑ Ensure that transfer, storage and use are tracked
- ❑ Screen personnel with access
- ❑ Required entities in possession of Select Agents to:
  - ❑ Develop/implement effective bio-safety programs
  - ❑ Develop/implement effective physical security programs

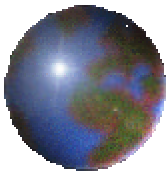
## **⊕ 42 CFR 1003 Civil Penalties for non compliance**

- ❑ Individuals           \$250,000
- ❑ Others               \$500,000



# *Authorities under 42 CFR 73*

- ❑ HHS (CDC) has authority and responsibility for regulating activities to protect protect public health and safety (HSS Select Agents, 42 CFR 73.4)
- ❑ USDA has authority and responsibility for regulating activities to protect animal and plant health and animal and plant products (42 CFR 73.5)
- ❑ 'Overlap' Select agents subject to regulation by both groups; control by Interagency coordination



# *Definition of a Biological Select Agent (Part 1)*

- ☐ **Microorganisms**

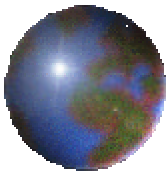
- ☐ including but not limited to bacteria, viruses, fungi, rickettsiae or protozoa

- ☐ **Infectious substances**

- ☐ any naturally occurring, bio-engineered or synthesized component of any such microorganism or infectious substance

- ☐ **Capable of causing**

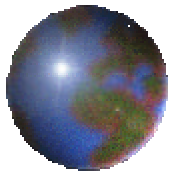
- ☐ death, disease or other biological malfunction in a human, an animal, a plant or another living organism
- ☐ deterioration of food, water, equipment, supplies or material of any kind
- ☐ deleterious alteration of the environment



## *Definition of a Biological Select Agent (Part 2)*

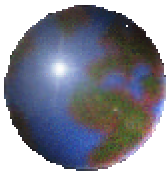
- ☐ **For which the HHS Secretary is concerned about:**
  - ☐ Effect on human health of exposure
  - ☐ Degree of contagiousness/method of transmission
  - ☐ Availability/Effectiveness of prevention/treatment
  - ☐ Any other criteria, e.g. needs of children and vulnerable populations





# Current List of Biological Select Agents

Agent Type	Viral	Bacterial	Fungal	Toxins
<b>HHS Select Agents</b>	<ul style="list-style-type: none"> <li>▪Crimean-Congo Haemorrhagic Fever Virus</li> <li>▪Ebola Viruses</li> <li>▪Cercopithecine Herpesvirus 1 (Herpes B Virus)</li> <li>▪Lassa Fever Virus</li> <li>▪Marburg Virus</li> <li>▪Monkeypox virus</li> <li>▪South American Haemorrhagic Fever Viruses (Junin, Machupo, Sabie, Flexal Guanarito)</li> <li>▪Tick-borne Encephalitis complex (Flavi) Viruses</li> <li>▪Variola Major Virus (Smallpox) and Variola Minor Virus (Alastrim)</li> </ul>	<ul style="list-style-type: none"> <li>▪<i>Rickettsia prowazekii</i></li> <li>▪<i>Rickettsia rickettsii</i></li> <li>▪<i>Yersinia pestis</i></li> </ul>	<ul style="list-style-type: none"> <li>▪<i>Coccidioides posadasii</i></li> </ul>	<ul style="list-style-type: none"> <li>▪Abrin</li> <li>▪Conotoxins</li> <li>▪Diacetoxyscirpenol</li> <li>▪Ricin</li> <li>▪Saxitoxin</li> <li>▪Tetrodotoxin</li> <li>▪Shiga-like ribosome inactivating proteins</li> </ul>
<b>Overlap Select Agents</b>	<ul style="list-style-type: none"> <li>▪Eastern and Venezuelan Encephalitis</li> <li>▪Nipah and Hendra Complex Viruses</li> <li>▪Rift Valley Fever Virus</li> </ul>	<ul style="list-style-type: none"> <li>▪<i>Bacillus anthracis</i></li> <li>▪<i>Brucella abortis</i>, <i>B. melitensis</i> and <i>B. suis</i></li> <li>▪<i>Burkholderia mallei</i> and <i>B. pseudomallei</i> (<i>Pseudomonas</i>)</li> <li>▪Botulism neurotoxin producing strains of <i>Clostridium</i></li> <li>▪<i>Coxiella burnetii</i></li> <li>▪<i>Francisella tularensis</i></li> </ul>	<ul style="list-style-type: none"> <li>▪<i>Coccidioides immitis</i></li> </ul>	<ul style="list-style-type: none"> <li>▪Botulism neurotoxins</li> <li>▪<i>Clostridium perfringens</i> epsilon toxin</li> <li>▪Shigatoxin</li> <li>▪Staphylococcal enterotoxins</li> <li>▪T-2 toxin</li> </ul>

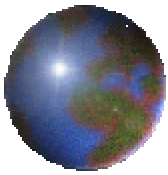


## *42 CFR 73.4 and 73.5*

### *Genetic Elements, Recombinant Nucleic Acids and Recombinant Organisms of Select Agents (SA)*

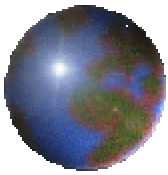
Additional details in Interim Regs

- ☐ (e)(1)
  - ☐ SA viral nucleic acids that can encode for infectious or replication competent forms of SA viruses
- ☐ (e)(2)
  - ☐ Nucleic acids (naturally derived or synthetic) that can encode for functional form of any of the SA toxins
- ☐ (e)(3)
  - ☐ Viruses, bacteria, fungi and toxins listed in 73.5 a-d (overlap SA) that have been genetically modified



## *Genetic Elements, Recombinant Nucleic Acids and Recombinant Organisms Considered Select Agents*

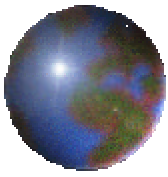
- ❑ Expanded (e)(1) viral nucleic acids from SA
  - ❑ naturally derived or synthetic
  - ❑ contiguous or fragmented
  - ❑ in host chromosomes or in expression vectors
  - ❑ that can encode for infectious or replication competent forms of SA viruses
- ❑ Expanded (e)(2) nucleic acids (naturally derived or synthetic) that can encode for functional form of any of the SA toxins
  - ❑ in a vector or host chromosome
  - ❑ that can be expressed *in vivo* or *in vitro*
  - ❑ are in a vector or host chromosome and can be expressed *in vivo* or *in vitro*



## *Exclusions Codified in the Interim Rule*

### **❑ General Exclusions across sections of 42 CFR**

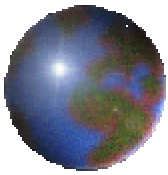
- ❑ Naturally occurring Toxins and SA; not introduced, cultivated collected or otherwise extracted from natural source
- ❑ Specific Vaccine Strains
  - ❑ Junin virus Candid #1, Rift Valley MP12, VEE TC-83
- ❑ Specific toxins when aggregate amount does not exceed certain milligram quantities
  - ❑ 0.5 mg Botulism Toxin, 5 mg Staph enterotoxin, 100 mg Shiga toxin
- ❑ Nonviable SA organisms or non functional toxins



# *What about...*

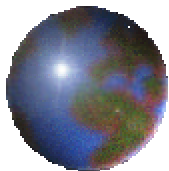
## ☐ Investigational New Drugs

- ☐ Subject to the SA regulation
- ☐ Must notify CDC of use
- ☐ Must notify CDC if there is a clinical hold
- ☐ Exemptions on case-by case basis



## *Exemptions from SA rule 42 CFR 73*

- ❑ **Exemptions for Agent and Facility**
  - ❑ Responsibility of the User/Entity to file
    - ❑ **Must apply to CDC or USDA, depending on the agent**
    - ❑ **Provide scientific information and justification for requested exemption**
    - ❑ **Must have specific procedures for use, transfer and destruction**
  - ❑ **CBER and other exclusions announced on Website**



# CDC Select Agent Program



## Select Agent Program

[SAP Home](#) | [Site Map](#) | [Contact Us](#)



### Program Links

Select Agent  
Regulations, 42 CFR  
73.0, Interim Final Rule

- [Application Information and Additional Forms](#)
- [General Information](#)
- [Helpful Resources](#)

Select Agent  
Regulation, 42 CFR  
73.6

- [Application Package](#)
- [Application Information](#)

Notification of  
Possession

Additional Resource  
Material

[Contact Us](#)

Search SAP



The Centers for Disease Control and Prevention is required to regulate the possession of biological agents and toxins that have the potential to pose a severe threat to public health and safety. CDC's Select Agent Program oversees these activities. The Select Agent Program currently requires registration of facilities including government agencies, universities, research institutions, and commercial entities.

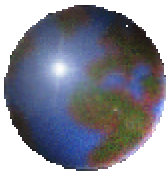
On this Web site you will be able to download application packages, view current regulations regarding select agents and access additional resource information. If you still have questions or concerns after reviewing the material contained in this website, please contact our program via email at [lsat@cdc.gov](mailto:lsat@cdc.gov), phone at 404-498-2255 or fax at 404-498-2265.

Materials on this site last updated: 07/10/2003 04:48 PM

**Attention Dermatologists:** Botulinum neurotoxin is only considered a select toxin under the Select Agent regulations when the amount under the control of a physician exceeds 0.5 mg. Additionally, all dermatology clinics using FDA-approved botulinum toxin preparations in accordance with labeling instructions are excluded from the requirements to register under the Select Agent regulations and DO NOT need to submit a letter to CDC or USDA to declare exemption from registration with the Select Agent Program.

### Select Agent Regulation, 42 CFR 73.0, Interim Final Rule

- [Application Information and Additional Forms](#)
  - [Application Package](#)
  - [Additional Forms](#)
- [General Information](#)
  - [Letter of Solicitation](#)
  - [Public Comments on the New Regulation](#)
  - [Public Meeting, Washington, DC, December 16, 2002](#)
  - [Regulatory Impact Analysis and Appendices](#)
- [Helpful Resources](#)
  - [FAQ for New Regulation \(updated 07/08/2003\)](#)
  - [List of Select Biological Agents and Toxins](#)
  - [Notification of Exclusion \(updated 06/12/2003\)](#)



# *USDA Select Agent Information*

## ☐ **USDA/HHS Select Agricultural Agents**

☐ [www.aphis.usda.gov/vs/ncie/bta.html](http://www.aphis.usda.gov/vs/ncie/bta.html)

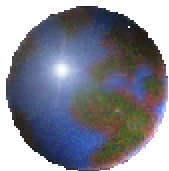
**(APHIS is the Animal & Plant Health inspection Service)**

☐ Regulated under Animal Protection Act

☐ Use is Regulated under USDA rather than CDC

☐ Links to CDC information





# USDA APHIS Information



## Veterinary Services

### Safeguarding Animal Health

#### Import / Export

Fri Sep 26 15:00:17 2003

#### Agricultural Bioterrorism Protection Act of 2002 Biological Agents and Toxins; Possession

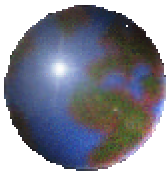
- [HHS, USDA Establish New Regulations for Use of Select Biological Agents of 2002 \(pdf\)](#)
- [December 13, 2002, Agricultural Bioterrorism Protection Act of 2002; Possession, Use and Transfer of Biological Agents and Toxins; Interim Final Rule, Department of Agriculture, APHIS \(pdf\)](#)
- [Agent and Toxin List \(pdf\)](#)
- [December 13, 2002, Possession, Use, and Transfer of Select Agents and Toxins; Interim Final Rule, Department of Health and Human Services, Office of the Inspector General \(pdf\)](#)
- [August 12, 2002 Federal Register Notice - Agricultural Bioterrorism Protection Act: Biological agents and toxins; possession](#)
- [Public Health Security and Bioterrorism Preparedness and Response Act of 2002 \(pdf\)](#)
- [Questions and Answers](#)

#### FORMS

- [APHIS Form 2044/CDC Form 0.1319 - Application for Laboratory Registration](#)

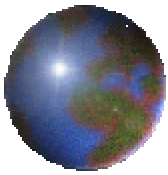
- [Attachment 1:](#) 42 CFR Part 75, Select Biological Agents and Toxins; Final Rule; Federal Register, December 13, 2002.
- [Attachment 2:](#) 9 CFR Part 121 - Agricultural Bioterrorism Protection Act of 2002; Possession, Use, and Transfer of Biological Agents and Toxins; Federal Register, December 13, 2002.
- [Attachment 3:](#) 7 CFR 331 - Possession of Select Agents; Federal Register, December 13, 2002.
- [Attachment 4:](#) APHIS application for permit to import or transport controlled material or organisms or vectors (VS forms 18-21)
- [Attachment 5:](#) Additional Information for cell cultures and their products (VS forms 16-7)

In order to fulfill the Department of Justice responsibilities under the Act, the Federal Bureau of Investigation (FBI) is responsible for conducting security risk assessments of individuals seeking access to listed agents and toxins and individuals or entities seeking to register under the Act.



## *Transport or Export of SA*

- ❑ 42 CFR 73 has a Procedural impact on actual transportation of Biological Select Agents
- ❑ 42 CFR 73 places no restrictions on exportation of SA or toxins
- ❑ **Shipping/Transport in the US**
  - ❑ Department of Commerce 15 CFR
  - ❑ Department of Transportation 49 CFR 171-178
    - ❑ IATA, ICAO, Individual Commercial Carriers
  - ❑ CDC revising 42 CFR 72 to harmonize other regs



## *Stay Tuned for More Info.....*

- ❑ **Frequent updates on various Websites**
  - ❑ Changes in status/ additions/deletions
  - ❑ Exclusions (Sterne Strain, FVS)
  - ❑ Revisions to 42 CFR 72 (shipping) expected soon
- ❑ **Direct Information from CDC/USDA**
  - ❑ Reviewed on a case-by case basis
  - ❑ Timely Review
- ❑ **Institutional Safety Committees/Officers/Scientists**
  - ❑ Registration, access/training, security, risk assessments, procedures